Prehabilitation: how to prepare our patients for elective major abdominal surgeries?

Pré-habilitação: como preparar nossos pacientes para cirurgias abdominais eletivas de maior porte?

CAROLINA GOMES GONÇALVES¹; ANNE KAROLINE GROTH¹

ABSTRACT
Surgical approach is the main form of treatment for several diseases of the abdominal cavity. However, surgical procedure itself is a stressor that may lead to adverse effects unrelated to the treatment goal. Prehabilitation has emerged as a multifactorial preoperative health conditioning program, which promotes improvement in functional capacity and postoperative evolution. The present study reviews literature using MEDLINE, Ovid, Google Scholar, and Cochrane databases in order to determine the concept of prehabilitation program and the indications and means of patient selection for it, as well as to suggest ways to implement this program in cases of major abdominal surgeries.


INTRODUCTION
Surgical interventions are indicated for the cure or palliation of numerous diseases. However, surgery itself represents a stress event that often leads to adverse effects unrelated to treatment goals. These adverse effects have a profound negative impact on the ability to perform daily activities and may impair patients' quality of life in the postoperative period¹-³.

Despite advances in surgical techniques, anesthesia, and perioperative care, a significant group of patients does not rapidly recover functional and physiological capacities, and about 30% of patients undergoing major abdominal surgeries have postoperative complications⁴. In addition, the increase in life expectancy has led to an increasing number of elderly patients requiring surgical treatments⁵.

Investigations on modifiable risk factors have identified some protective factors for surgical complications and postoperative recovery, such as good fitness and functional reserve and nutritional status improvement⁶-⁸.

The deterioration of these parameters is associated with a higher incidence of surgical complications and need of intensive care⁹-¹², what has led to the implementation of preoperative strategies to promote protective factors and eliminate risk factors related to surgical procedures. These preoperative conditioning or surgical prehabilitation measures are important to counteract the expected decline in physical function and overall well-being associated with surgery.

Good functional capacity is directly related to postoperative evolution¹³,¹⁴, as well as other factors that can be addressed in a multifactorial intervention, such as structured physical exercises, nutrition optimization, psychological support, combat of anemia, and interruption of negative health behaviors¹⁵,¹⁶. Patients undergoing major abdominal surgeries for gastrointestinal, gynecological, hepatobiliary, and pancreatic neoplasms may in particular benefit from prehabilitation, with main focus on factors such as cachexia, myopenia, and sarcopenia, all associated with poor long-term postoperative outcome¹⁷.

¹ - Positivo University, School of Medicine, Curitiba, PR, Brasil.
This review article aims to clarify the definition and benefits of prehabilitation and the indications and means of patient selection for it in cases of major gastrointestinal surgeries, as well as to establish a proposal of a multifactorial prehabilitation approach so that these measures are increasingly incorporated into surgeons' clinical practice.

**Definition and history of prehabilitation**

Prehabilitation is defined as the process of expanding patient's functional and psychological capacity to reduce potential deleterious effects of a significant stressor, which is the surgical procedure itself\(^\text{18}\). Following the traditional approach of rehabilitation, initial prehabilitation interventions have primarily focused on improving preoperative physical function of patients undergoing orthopedic, cardiac, and neoplastic surgeries\(^\text{19}\). Most of the initial studies have been performed on patients undergoing cardiovascular surgeries and the results of physical prehabilitation have shown improvement in cardiac function, breathing, and postoperative functional capacity\(^\text{20-22}\). Quality studies and systematic reviews have demonstrated the positive impact of preoperative exercise programs on the improvement of physical function, quality of life, postoperative complications, and length of hospital stay\(^\text{7,23,24}\). However, the benefit of prehabilitation has been questioned in another systematic review\(^\text{25}\), justified by the lack of standard in physical activity programs, the diversity of surgeries performed in the studies, and the restriction to physical activity, not including nutritional and psychological interventions in many studies.

These findings have suggested that improving physical activity alone could not be sufficient and that prehabilitation should also include preoperative nutrition and measures to reduce stress and anxiety. The definition of pre-surgical conditioning has then evolved to incorporate a multidisciplinary approach aimed at improving the clinical course of the disease, preventing specific damage caused by the disease, such as neoplasms, identifying dysfunctions, and finally introducing measures capable of reducing the incidence and/or severity of future dysfunctions, determining the improvement of physical condition and nutritional status and reducing preoperative anxiety.

It is important to distinguish between preoperative conditioning and enhanced postsurgery recovery programs, such as Enhanced Recovery After Surgery (ERAS), which employ intra- and postoperative care plans with the intention of accelerating recovery. ERAS may incorporate prehabilitation, but this itself represents a broader surgical recovery approach. Prehabilitation groups measures applied in the preoperative period in order to improve patients' functional performance, hoping to reduce morbidity and mortality, and accelerate postoperative recovery. The idea of prehabilitation is to optimize the health of the patient who will be subjected to a controlled aggression, i.e., the surgery. All measures that promote the improvement of the patient's physical and mental health can be included in the prehabilitation process.

**Which patients benefit from prehabilitation? Those requiring major abdominal surgeries?**

Major surgeries induce an increased systemic inflammatory response that promotes...
lean muscle loss, homeostatic imbalance, and aerobic capacity decrease. In addition, patients with low cardiorespiratory reserve cannot meet the increase of postoperative oxygen demand. Studies have already demonstrated that preoperative cardiorespiratory fitness has been associated with good postoperative outcome following major intra-abdominal surgeries\textsuperscript{23}. In a randomized study by Gillis \textit{et al}.\textsuperscript{15}, 80\% of patients who had received multimodal prehabilitation prior to colorectal cancer resection surgery have recovered their baseline functional capacity by eight weeks post-surgery, compared to only a 40\% recovery rate in a historical control that had received only postoperative rehabilitation\textsuperscript{26}. More recently, Barberan-Garcia \textit{et al}.\textsuperscript{27} have demonstrated that personalized prehabilitation has reduced the number of patients with postoperative complication by 51\%, when evaluating high-risk patients undergoing elective major abdominal surgery. There is a growing acceptance that the success of a surgery does not depend solely on the procedure itself, but mainly on how quickly the patient is able to return to his or her physical and psychological state of health. Although there are no conclusive evidences, there are indications that prehabilitation plays an important role in patient recovery by decreasing the risk of postoperative complications, especially in populations at increased risk\textsuperscript{27} or those that will undergo major surgeries.

Based on the concept that increasing physiological reserve before surgery, and not after, promotes better functional capacity throughout perioperative and recovery periods, it makes sense to indicate prehabilitation for those in need of special care, such as the elderly, patients with some frailty, or those at risk of malnutrition. Elderly patients have more postoperative complications and longer convalescent periods than young patients. Surgical morbidity and mortality increase exponentially after 75 years of age\textsuperscript{28}. Studies suggest that patients with lower baseline functional capacity during the walk test are more likely to achieve significant improvements in physical function through prehabilitation\textsuperscript{29}. A recent study has demonstrated that elderly patients whose 6-minute walk test (6MWT) results have been below 400 meters (above 400 meters indicates independence and mobility) have responded to multimodal prehabilitation with a 10\% to 15\% increase in baseline functional capacity during preoperative period and after surgery\textsuperscript{29}. Some authors point out that, to be cost-effective, preoperative exercise programs should only be indicated for high-risk patients, i.e., those with low cardiopulmonary reserves (aerobic threshold $<11\text{ml/kg/min}$). Thus, preoperative risk stratification protocols which consider cardiopulmonary exercise stress test (CPET) values, determining cardiopulmonary reserve, should be established to properly select patients who will benefit from prehabilitation program\textsuperscript{30}. On the other hand, patients undergoing complex treatments for gastrointestinal neoplasms, or major abdominal surgeries, are probably already included in the selection of patients who will have high cost-benefit with prehabilitation program. Appropriate patient selection has not been defined yet, but there are no reports of harms brought by prehabilitation program. Therefore, the current recommendation may include all patients requiring major abdominal surgery.
Preoperative assessment to determine the need for prehabilitation

Exercise

The assessment of cardiorespiratory fitness is essential to determine the indication of prehabilitation for patients who will undergo major abdominal surgeries. Cardiorespiratory reserve can be measured objectively using CPET. This test provides an objective analysis of the functional integration of the cardiovascular, respiratory, hematic, and cellular systems by measuring gas exchange-derived variables, such as oxygen consumption in anaerobic threshold (AT) and at peak exercise (VO₂ max). Studies have shown an association between low AT and postoperative complications after major noncardiac surgeries. Due to its accuracy, the future selection of patients who will benefit most from prehabilitation programs will probably have CPET variables as criteria.

Recent studies have also used the 6MWT to predict postoperative morbimortality. This test is one of the best functional indicators in old individuals who can benefit greatly from prehabilitation. The test is simple and inexpensive and assesses how far the patient can walk in six minutes. The patient should walk a long, flat 30-meter course as many times as possible at his or her own pace, stopping to rest if necessary. The test technician notes the heart rate, presence or absence of dyspnea, fatigue levels at the beginning and end of the test, distance covered, whether the test has been finished prematurely and the reasons for this (angina, severe dyspnea etc). Test repetition after prehabilitation exercises allows the quantification of changes in baseline functional capacity.

Nutrition

Nutritional status assessment can be performed using global subjective assessment (GSA) and Nutritional Risk Screening Tool (NRS2002). A GSA-B (suspected of malnutrition or mild or moderate malnutrition) or C (severe malnutrition) determines the indication for intervention. NRS2002 scores ≥3 characterize risk of malnutrition and thus also indicate nutritional support through prehabilitation programs.

Psychological well-being

Major surgeries cause physical and mental stress for patients and therefore psychological assessment is of great importance. Most articles use Hospital Anxiety and Depression Scale (HADS), which includes two subscales, anxiety and depression, each with seven items that are scored from 0 to 3. A score >8 on each of the subscales suggests the presence of mood disorders. A stratified approach may also be needed to determine the patients who will benefit from psychological prehabilitation. However, this would require a routine psychological assessment in the preoperative period, which is not the current practice in abdominal surgeries, except for bariatric surgeries.
Clinical assessment

Complete preoperative clinical assessment cannot be forgotten when risk factors, such as smoking, anemia, diabetes mellitus, and other comorbidities, can be identified and controlled.

How to implement prehabilitation?

Physical exercises

Physical exercise is the basis of all initial prehabilitation programs. Its goal is to improve the patient’s functional capacity through structured regimens that include aerobic, resistance, muscle strengthening, flexibility, and balance training. Exercise prescription should be adapted according to the 6MWT, VO₂ max test and AT test. Within the context of prehabilitation, interventions usually apply systemic or tissue-specific (therapeutic) exercises, depending on the disease and possible treatment-related sequelae. The first approach, which includes systemic exercises, addresses the expected loss of cardiovascular and musculoskeletal capacity that occurs after prolonged periods of sedentary behavior, such as immobilization before and after surgery. Tissue-specific exercise is beneficial for localized morbidities and could include deep and diaphragmatic breathing exercises for thoracic surgeries, or knee flexion-extension exercises for orthopedic surgeries.

The World Health Organization’s recommendation to the general population includes 150 minutes of moderate activity or 75 minutes of vigorous physical activity per week. This can be safely performed for patients who will undergo major abdominal surgeries, unless there is some specific contraindication. Patients who qualify for prehabilitation programs should receive individualized prescription of physical exercises, which should be appropriate to their needs and physiological status.

The exercise prescription should specify the frequency, intensity, time, and type of physical activity to be performed. In general, the 150 minutes per week should be divided into 30- to 40-minute aerobic exercise sessions, twice to three times a week, with moderate-intensity level (50-75% of the predicted maximum heart rate for age or Borg scale of 12-16, for example). Exercise can be walking, cycling, swimming, depending on patient’s availability and preference. Besides aerobic exercises, muscle-strengthening exercises should be performed using appropriate equipment and under the control of a physiotherapist or physical educator, at least twice a week, focusing on strengthening all muscle groups required in daily life (arms, shoulders, chest, abdomen, back, hips, and legs). Flexibility and balance exercises are also encouraged as part of prehabilitation training program.

The ideal exercise regimen has not been defined yet. This explains the diversity of prehabilitation programs in literature. Exercise intensity optimization can be performed by monitoring heart rate or by using Borg scale (Figure 1), which is a subjective tool used during exercise to estimate effort based on how strenuous the exercise is.
The intensity of the exercise is adjusted to achieve the proposed goals, usually 12-16 in prehabilitation programs. This scale correlates very well with heart rate, ventilatory rate, serum lactate, and VO₂ max. When heart rate is used as the assessment method, the heart rate zone should be between 70% and 80% of the maximum heart rate for age.

**Nutritional optimization in prehabilitation**

The nutritional status of patients scheduled for abdominal surgeries is directly influenced by the presence of neoplasms, age, chemotherapy, and disease stage. Therefore, nutritional status screening should be performed in all patients who will undergo major abdominal surgeries. Nutritional therapy should be provided to all patients at risk for complications induced by malnutrition during perioperative period. Patients classified as malnourished or at high risk for malnutrition should receive seven to 14 days of nutritional support, preferably enteral, during preoperative period, even if this delays the treatment of neoplasms. Well-nourished patients who will undergo major surgeries with many risks may also benefit from nutritional support.

Proper nutrition requires enough quantities of protein to promote anabolism and enough energy to maintain body weight in situations of major metabolic stress. The recommended protein intake in healthy adults is of 0.8g of protein per kilogram of body weight a day, but the need in surgical patients may increase to 1.2g to 1.5g of protein per kilogram of body weight a day. Patient should receive nutritional guidance, which aims the daily ingestion of two protein servings, ranging from 20 to 40 grams.

If the patient is unable to ingest dietary recommendations, he (she) should be advised to take protein supplements. Patients should be instructed to ingest protein or supplements within one hour after physical exercise in order to use the “anabolic window”, i.e, the period in which muscle protein synthesis is at its peak. Carbohydrates can also be given few hours before physical activity, because they increase muscle and liver glycogen, facilitating physical exercises proposed by prehabilitation.
At least 140g of carbohydrate three hours before working out facilitate physical exercise performance, and 10g of protein after working out increase dynamic muscle strength by 25%\(^9\). Non-protein components of the diet, such as fat, carbohydrates, fibers, and micronutrients, should also be properly integrated. Recommendations for preoperative nutrition and immunonutrition are standardized, so prehabilitation should follow these recommendations.

**Interventions for psychological well-being**

Prehabilitation protocols advocate an initial assessment to identify patients in need of psychological intervention, and subsequently guidance on stress and anxiety reduction techniques, such as relaxation techniques and breathing exercises for all patients.

Psychological stressors, such as diagnosis, surgery, anesthesia, pain, survival, and recovery, are all worry and anxiety causes which may affect recovery after surgery by various mechanisms. Negative emotions may increase the sensation of pain or may influence behavior (perform physiotherapy, take painkillers). On the other hand, preoperative stress is associated with slower healing through the interaction of psychological and immunological processes\(^50,51\). Anxiety, depression, and low self-esteem are constantly associated with worse physiological outcomes and quality of life after surgeries. Anxiety is related to worse short-term postoperative outcome and longer hospital stay, while depression is related to long-term pain\(^52,53\).

There are many evidences which support the role of psychological prehabilitation before surgery from randomized clinical trials in patients with breast, colon, and prostate neoplasms. In these studies, preoperative interventions, such as relaxation techniques (deep breathing, progressive muscle relaxation, meditation), have shown a positive effect on pain intensity and postoperative quality of life\(^54\).

In a recent meta-analysis, Powel et al.\(^55\) have reported that evidences suggest that psychological preparation may be beneficial for postoperative pain, behavioral recovery, negative affect, and length of hospital stay. However, the quality of evidences has been low or very low and insufficient to be used as a practical recommendation. It is noteworthy that in most evaluated studies psychological preparation has been performed in isolation and not as multifactorial prehabilitation and intervention time has been quite varied.

In the most recent multimodal prehabilitation studies, psychological preparation consists of a 60- to 90-minute consultation with a psychologist and training in relaxation techniques and breathing exercises, besides the delivery of material with exercise videos to be carried out at home\(^26,56\). The primary goal of the psychological component is to broaden and reinforce patients’ motivation to commit to the nutritional and physical exercise aspects of the program.

Cognitive trainings in the form of psychological counseling, meditation, or yoga may also reduce perioperative anxiety and stress\(^53\) and be the area of study for new multifactorial prehabilitation protocols.

Psychological prehabilitation, inserted in multifactorial prehabilitation and with the objective of decreasing anxiety and depression, as well as increasing coping skills, has shown no bad effects either\(^26\). Thus, new approaches to stress reduction and psychological support should be more systematically evaluated, determining the best form of intervention to be included in prehabilitation programs.
Comorbidity and risk factor optimization

Anemia

Anemia is defined as a hemoglobin concentration <13g/dl in men and <12g/dl in women at sea level. Oxygen delivery to tissues depends on arterial oxygen concentration and cardiac output. Therefore, oxygen delivery may be compromised by low hemoglobin concentration. Normal levels of oxygen delivery to tissues may be maintained up to hemoglobin concentrations of 6-10g/dl, as the decrease of blood viscosity increases blood flow. Tissue hypoxia occurs below these levels. Preoperative anemia is associated with the increase of postoperative morbidity and is directly related to red blood cell transfusion in surgeries with moderate or severe blood loss. Blood transfusion, in turn, has a negative impact on survival rates in colorectal neoplasms. The presence of anemia should be investigated in all patients who will undergo moderate- to high-risk bleeding surgical procedures (>500ml). Serum ferritin levels below 30ng/ml are the most sensitive and specific method for identifying iron deficiency.

Preoperative anemia should be treated with oral or intravenous iron. The goal should be to achieve hemoglobin levels above 13g/dl. Iron should be administered orally (40 to 60 mg, daily). Patients with intolerance to oral administration or in situations where surgery is planned for less than six weeks after diagnosis of iron deficiency should receive intravenous iron.

Glycemic control

Preoperative glycated hemoglobin has been proposed as a biological prognostic marker in surgical patients, and levels greater than 7% indicate inadequate glycemic control and increase the risk of preoperative complications. Prehabilitation program should address glycemic changes, even if this means postponing surgery, since preoperative glycemic control is associated with a reduction of infectious complications.

Smoking cessation

Smoking has a transient effect on the tissue microenvironment and a prolonged effect on inflammatory and reparative cell functions leading to delayed healing. Smoking is a known risk factor for postoperative complications and should therefore be discontinued for more than four weeks prior to surgery in order to reduce postoperative complications. Smoking cessation program should include counseling and pharmacological therapy with nicotine or bupropion. The role of smoking cessation in the context of multimodal prehabilitation has been little explored, and evidences suggest some beneficial effects. Future studies should also explore whether participating in multimodal prehabilitation programs rather than isolated smoking cessation programs may result in better postoperative outcomes or even successful smoking cessation.

What is the ideal duration of surgical prehabilitation?

The optimal duration for prehabilitation program should be determined by the best relationship between program adherence and effectiveness. Prehabilitation program from two to four weeks seems to be inefficient, while exceeding three months in duration may have poor patient adherence. If the underlying disease allows, the duration of prehabilitation should be from four to eight weeks.
Timmerman et al.\textsuperscript{64} have shown that, in patients awaiting surgery for cancer, five weeks of preoperative exercise have been sufficient to record significant improvement in cardiorespiratory preparation and muscle strength. Exercise and training limitations due to pain may prolong the time required for the increase of physical resistance. In cancer patients, there is a greater limitation for performing longer prehabilitation programs, but a period from four to six weeks of prehabilitation may be appropriate to increase physiological reserve\textsuperscript{65}. Therefore, the accumulation of evidences suggests that prehabilitation period should probably be longer than four weeks.

**Multimodal/multifactorial intervention**

We made a short intervention proposal that includes the following items in the prehabilitation program of 4-8 weeks: 1) individualized physical exercises; 2) nutritional optimization; 3) intervention for psychological well-being; and 4) health optimization. Each of the variables requires screening methods and specific intervention measures summarized in figure 2.

**How to evaluate the benefits of prehabilitation?**

The objectives of prehabilitation are the following: to reduce postoperative complications, increase recovery speed, and improve patients’ quality of life. In addition, measuring adherence to programs is also vital in order to assess their effect. Results of prehabilitation program need to be evaluated through objective and subjective parameters before surgical procedure, after program implantation, and after initial postoperative period. Proposed periods are usually immediately before surgery (1-2 days before) and eight weeks after surgery.

Adherence to multimodal prehabilitation program should be specified in each of its components and measured as the percentage of participation in the suggested interventions (attending physical exercise trainings, performing adequate protein intake, performing relaxation techniques, etc.). Postoperative complication rates are fundamental for program evaluation. Postoperative complication reduction is usually very heterogeneously evaluated and, therefore, Bruns et al. have suggested the implementation of Comprehensive Complication Index (CCI), which calculates the sum of morbidities and mortality presented on Clavien-Dindo scale\textsuperscript{66,67}. Measurements of functional capacity and cardiopulmonary function (6MWT and CPET) are also fundamental to identifying improvement in physical fitness and functional capacity after prehabilitation programs. Finally, psychological (HADS) and quality-of-life reassessments through the use of validated questionnaires can help identify patients and procedures that may have the greatest benefit and determine the risk stratification required for patient selection.

![Figure 2. Multimodal prehabilitation scheme.](image)
Future targeting

Many recent systematic reviews have studied isolated prehabilitation programs which have used solely physical activity interventions\textsuperscript{68}, nutrition optimization or immunonutrition\textsuperscript{69,70} or psychological optimization\textsuperscript{54}. Despite the importance of these studies, since the implementation of early recovery programs (ERAS), the importance of multimodal programs for synergistic benefit gain has been emphasized\textsuperscript{71}. Although recent, the multimodal approach to prehabilitation has already several significant studies. Li et al.\textsuperscript{26} have identified that a 1-month trimodal prehabilitation program in colorectal cancer patients has improved postoperative recovery and functional capacity. Giilis et al.\textsuperscript{15} have demonstrated that patients who underwent trimodal pre-habilitation for four weeks before surgery and who continued for eight weeks after surgery had better functional capacity than patients who underwent rehabilitation for only eight weeks after surgery.

The current direction is that prehabilitation programs should be structured and customized for each patient. Therefore, it is necessary to consider the type of surgery, patient’s current state of health, and current state of the disease. Given the potential costs of multimodal prehabilitation programs, it makes sense to target these programs to populations that can benefit most constantly in relation to postoperative evolution. Intuitively, elderly and frail patients, as well as those with many comorbidities, should be identified as target audience for prehabilitation, which should always be offered to them.

Following the same principle, major abdominal surgeries also carry significant risk even in healthy patients with good functional reserve, since the extent and duration of stress response are proportional to the magnitude of surgery and are associated with increased risk of postoperative complications.

It is clear that the emerging model of surgical prehabilitation will involve a multifactorial and interdisciplinary approach. The optimization of comorbidities and patients’ education regarding surgery should be accompanied by physical, nutritional, and psychological optimization. Preoperative risk stratification is fundamental and depends on multidisciplinary collaboration for decision-making on program implementation. But, mainly programs will need to be individualized and patients be supported by healthcare staff through phone calls, applications or other forms of motivation and feedback, to stimulate or even modify or regulate the program, when needed.

Major surgeries are like marathons, therefore, patients need to be strategically prepared for them. Preoperative period is the key moment to direct treatment measures and prevention of modifiable risk factors. Developing reproducible methods and defining standardized outcome analysis tools will help establish a solid base for individualized prehabilitation programs for each patient.
RESUMO

Várias doenças da cavidade abdominal têm, na abordagem cirúrgica, sua principal forma de tratamento. Entretanto, o próprio procedimento cirúrgico é um agente estressor que pode promover efeitos adversos não relacionados com o objetivo do tratamento. A pré-habilitação emergiu como um programa multifatorial de condicionamento de saúde pré-operatório, que promove melhora na capacidade funcional e na evolução pós-operatória. O presente estudo faz uma revisão da literatura usando os bancos de dados MEDLINE, Ovid, Google Scholar e Cochrane para determinar o conceito, as indicações, os meios de seleção dos pacientes, e para sugerir as formas de implementação do programa de pré-habilitação em cirurgias abdominais de grande porte.


REFERENCES


Received in: 06/15/2019
Accepted for publication: 07/10/2019
Conflict of interest: none.
Source of funding: none.

Mailing address:
Carolina Gomes Gonçalves
E-mail: carolgg@gmail.com
carolina.goncalves@up.edu.br